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1235 '00 APR 11 A9:54

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

7 April 2000

RE: Docket No. 00D-0084
Guidance for Industry – Special Protocol Assessment

Dear Sir/ Madam,

Pharmacia and Upjohn appreciates the opportunity to review the *draft* Special Protocol Assessment Guidance.

We would like to take this occasion to note that some of the benefits that this guidance will make available have, in large part, already been possible with Agency divisions who encourage transparent communication with sponsors. At the same time, this guidance will be useful in working with areas of the FDA who have not always supported this type of dialog.

Please note the following two recommendations:

- **We recommend consideration be given to remedies that would allow FDA to fully respond to a sponsor within 45 days of the Agency's receipt of a clinical protocol--even when an Advisory Committee is consulted.**

  It is important for the patients that regulators and pharmaceutical firms work together to expedite drug development as much as possible. In this regard, both our pharmaceutical development and preclinical scientists were comfortable with the proposed guidance. With careful planning, even if need for a special protocol assessment is necessary, it should be possible to keep both stability protocols and carcinogenicity studies off the critical path to drug launch.

  However from a clinical perspective, should a special protocol assessment be needed, it could in large part, if not in total, take place on the critical path. In this respect, we are particularly concerned about the timing should it be decided that Advisory Committee review is necessary (references lines 188 through 202). In this case, we could foresee that 180 days or more could be consumed by the special protocol review (eg, 45 days for FDA to inform a sponsor that advice will be sought from an Advisory Committee, 90 days until the Advisory Committee Meeting, and 45 days for FDA to provide their response to the sponsor).

  We note that the 12 November 1997 letter from Donna E Shalala to Senator James M. Jeffords envisioned a response within "45 days of Agency receipt of the protocol and the questions. ..." When an Advisory Committee is consulted, the process described will not achieve this timeframe. Perhaps other mechanisms could be used to obtain advice from the Advisory Committee members. Perhaps it would be possible to shorten the timeframes for the various activities involved.

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- **We recommend omitting the limitations regarding general development strategies and issues (introductory phrase 132-133; 152-155).**

  The above-mentioned Shalala letter indicated that, "the agency would evaluate certain protocols and issues to assess whether the design is adequate to meet scientific and regulatory requirements identified by the sponsor." Consistent with this, the draft guidance notes that reasonable detail regarding data, assumptions, and information is needed by the Agency. For example, the sponsor is required to clearly describe any regulatory outcomes and final labeling which will be supported by the study (lines 136-138, with further FDA needs regarding clinical studies detailed through line 146).

  At the same time, the draft notes that general development issues, such as the number of trials needed or adequacy of supportive evidence for a given efficacy claim are not part of the special protocol assessment (lines 152-155). We could envision that this limitation would not allow the sponsor to find out if the "design is adequate to meet scientific and regulatory requirements identified by the sponsor" (quote from Shalala letter).

  We realize that ultimately the Agency must review an application in its totality (line 225) and understand that it is not always possible for FDA to agree if a specific finding will satisfy a specific objective (line 222-223). However, it would expedite drug development if sponsors could obtain early, written Agency agreement regarding general development strategies and issues in the context of a given protocol.

Again, thank you for the opportunity to comment. Should any clarification of our input be required, please don't hesitate to contact Jenny Peters at (616)-833-8141.

Sincerely,

PHARMACIA & UPJOHN COMPANY

Mark L. Mankel for

Jenny L. Peters
Director Regulatory Intelligence

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